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Date: Nov. 5 2001 By Deborah Huncate

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	John F. Stone	Docket No.:	36435.0100
Serial No.:	09/498,135	Filed:	February 4, 2000
		Examiner:	Enewold, T.
Title:	CHROMOSOME-BASED METHOD FOR FACILITATING DISEASE DIAGNOSIS	Group Art Unit:	1655

REQUEST FOR RECONSIDERATION

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Applicant hereby responds to the Office Action dated May 4, 2001, for which the period to respond is extended by three months to November 4, 2000. Because November 4, 2001, fell on a Sunday, this Response and Amendment is timely filed on the following Monday, November 5, 2001. Under separate cover, Applicant has also filed a Notice of Appeal, a copy of which is attached hereto. Applicant respectfully requests reconsideration and allowance of all pending claims.

35 U.S.C. § 103 Rejections

Claims 1-4, 6-8, 11, 13, and 15-17 stand rejected under 35 U.S.C. § 103 (a) as being unpatentable over Cherry et al. in view of Marcon et al., Mutation Research, Vol. 45, pp. 155-166, 1999. Applicant traverses this rejection.

Cherry et al. generally discloses that chromosome breakage is measured in metaphase by microscopic examination of broken chromosomes. In contrast to Applicant's claimed invention, Cherry et al. does not teach or suggest "produc[ing] chromosome fragments having broken ends ...and analyzing the marked broken ends within interphase cell nuclei" as set forth in claim 1, from which claims 2-4 and 6-7 depend; "marking at least a portion of the ends within interphase

nuclei" as set forth in claim 11, from which claims 13 and 15 depend; or "marking at least some of the ends within interphase nuclei" as set forth in claim 16, from which claim 17 depends. Rather, Cherry et al. teaches conventional cytogenetic techniques to count chromosome damage of chromosomes outside the cells' nuclei–such techniques are relatively labor intensive and expensive.

Marcon et al. generally discloses that broken DNA strands in interphase cell nuclei can be inferred from the splitting or diminution of signals generated by fluorescence *in situ* hybridization (FISH) for particular chromosomes in targeted regions (p. 163). The study described in Marcon et al. investigated the suitability for cytogenetic monitoring of benzene-exposed workers. In contrast to Applicant's claimed invention, Marcon et al. does not discuss disease diagnosis. In further contrast to Applicant's invention, ends of chromosome fragments are not labeled. Rather, portions of the chromosomes, whether they are intact or severed, are labeled. Thus, additional analysis is required to determine whether a particular chromosome is broken. Moreover, Applicant's invention may be used to analyze an entire genome, similar to Cherry et al., whereas Marcon et al. only teaches analysis of specific chromosomes in targeted areas.

Applicant also submits that nothing in either Cherry et al. or Marcon et al. teaches or suggests the combination of the two references. To establish a *prima facie* case of obviousness, the Examiner must establish that there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine reference teachings. In this case, Cherry et al. discloses a method that analyzes a whole genome in metaphase, whereas Marcon et al., discloses analyzing a small region of one or two chromosomes. Furthermore, Cherry et al. analyzes broken ends of DNA, whereas Marcon et al. does not. Neither reference suggests the analysis technique used in one reference would work for the analysis technique disclosed in the other reference. Moreover, Cherry et al. discloses a technique for disease diagnosis, whereas Marcon et al. simply discloses investigation of chromosome alterations in peripheral blood cells of Estonian petrochemistry workers. Thus, there is no suggestion to combine the references, and Applicant submits that the references are nonanalogous. Therefore, Applicant submits that the combination of the references is improper and the rejections to claims 1-4, 6-8, 11, 13, and 15-17 should be withdrawn.

Furthermore, neither Cherry et al. nor Marcon et al. disclose or suggest "3'—OH strands" as set forth in claims 6 and 15. Accordingly, claims 6 and 15 are additionally allowable over Cherry et al. and Marcon et al. Therefore, Applicant requests that the Examiner reconsider and withdraw her rejections to claims 6 and 15.

Claims 1-2, 4, 11, 13, and 16-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chen et al. in view of Marcon et al. Again, Applicant traverses this rejection.

Chen et al. discloses a technique for analyzing Alzheimer's disease that is similar to the technique disclosed in Cherry et al. Chen et al. does not disclose "produc[ing] chromosome fragments having broken ends ...and analyzing the marked broken ends within interphase cell nuclei" as set forth in claim 1, from which claims 2 and 4 depend; "marking at least a portion of the ends within interphase nuclei" as set forth in claim 11, from which claim 13 depend; or "marking at least some of the ends within interphase nuclei" as set forth in claim 16, from which claim 17 depends. In contrast to Applicant's claimed invention, Chen et al., similar to Cherry et al., discloses use of conventional cytogenetic techniques that involve chromosome preparation. Such labor intensive and expensive techniques are neither required nor claimed in the present application.

Nothing in either Chen et al. or Marcon et al. suggests the combination of the two references. The Examiner states that the combination the references would be obvious to one skilled in the art. Applicant traverses this statement. Chen et al. discloses a technique that analyzes an entire genome (similar to an embodiment of Applicant's invention and to Cherry et al.); whereas, Marcon et al. discloses a technique for analyzing specific regions on specific chromosomes. Furthermore, Marcon et al. does not teach that the method disclosed therein is suitable for disease diagnosis. Therefore, Applicant submits that the combination of the two references is improper and requests that the Examiner withdraw her rejection to claims 1-2, 4, 11, 13, and 16-17.

Claims 1-6 and 11-13, and 15-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Parshad et al. in view of Marcon et al. Applicant traverses this rejection. Similar to Chen et al. and Cherry et al., Prashad et al. does not disclose "produc[ing] chromosome fragments having broken ends ...and analyzing the marked broken ends within interphase cell nuclei" as set forth in claim 1, from which claims 2-4 depend; "marking at least a portion of the ends within interphase nuclei" as set forth in claim 11, from which claims 12-15

depend; or "marking at least some of the ends within interphase nuclei" as set forth in claim 16, from which claim 17 depends. In contrast to Applicant's claimed invention, similar to references noted above, Parshad et al. discloses use of conventional cytogenetic techniques that involve chromosome preparation. Thus, for the reasons cited above, nothing in either Parshad et al. or Marcon et al. teaches or suggests the combination of the two references. Furthermore, it would not be obvious to one skilled in the art to combine the references because the two references teach two different and distinct methods of analyzing portions of a cell.

Finally, claims 8-10 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cherry et al. in view of in view of Marcon et al., and in further view of Gorczyca et al. Again, Applicant traverses this rejection because none of Cherry et al., Marcon et al., Gorczyca et al., or a combination thereof, teach or suggest combining any of the references. Gorczyca et al. teaches that broken *ends* of DNA can be labeled *in situ* with terminal deoxynucleotide transferase (TdT). The technique taught in Gorczyca et al., is used to detect apoptosis or programmed cell death. Apoptosis is not a disease state. Cherry et al., teaches that a disease state can be detected from direct observation of broken chromosomes. Marcon et al. does not disclose marking ends of chromosomes or disease diagnosis; rather, Marcon et al. teaches marking of various portions of chromosomes. Thus, nothing in the references teaches or suggests the combination of the references. Furthermore, even if the references were combined, the combination does not teach or suggest the claimed invention because the combination does not result in "a method suitable for facilitating disease diagnosis" including the "analyzing the marked broken ends within interphase cell nuclei" as set forth in claim 1, from which claims 8-10 depend.

In view of the foregoing arguments, Applicant submits that all pending claims are allowable over the cited references. Applicant therefore earnestly solicits allowance of pending claims 1-13 and 15-17. The undersigned would welcome a telephone call at the telephone number listed below if such would advance prosecution of this application.

Respectfully submitted,

By: 

Scott M. Smith
Reg. No. 48,268

SNELL & WILMER L.L.P.
One Arizona Center
400 East Van Buren
Phoenix, Arizona 85004-0001
(602) 382-6296
36435.0100\SMITHSM\PHX\1091942